FILE 'REGISTRY' ENTERED AT 13:29:56 ON 13 JUL 2009 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2009 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 12 JUL 2009 HIGHEST RN 1161919-42-1 DICTIONARY FILE UPDATES: 12 JUL 2009 HIGHEST RN 1161919-42-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2009.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

```
=> e azd2171
           60
E.1
                   AZD/BI
Ε2
            1
                  AZD1152/BI
E3
            0 --> AZD2171/BI
             1 AZDB/BI
E4
                 AZDDMEC/BI
E5
            1
            1 AZDDU/BI
1 AZDEL/BI
1 AZDGTP/BI
1 AZDH/BI
2 AZDI/BI
1 AZDIENE/BI
Ε6
E7
E8
E9
E10
E11
E12
            1
                  AZDIMYCIN/BI
=> e cediranib/cn
            1
                  CEDIN/CN
E2
             1
                  CEDINOL/CN
E3
             1 --> CEDIRANIB/CN
                 CEDIRANIB MALEATE/CN
E4
             1
                  CEDKATHRYN A/CN
E5
             1
                 CEDKATHRYN B/CN
E.6
            1
                 CEDMILIN/CN
E7
            1
            1
                  CEDMILINE/CN
E8
            1
                  CEDMILINOL/CN
E9
            1
                  CEDO 8811/CN
E10
            1
                  CEDO 8816/CN
E11
            1
E12
                  CEDO 8834/CN
=> e3
L1
             1 CEDIRANIB/CN
=> d 11
    ANSWER 1 OF 1 REGISTRY COPYRIGHT 2009 ACS on STN
T.1
RN
     288383-20-0 REGISTRY
ED
    Entered STN: 08 Sep 2000
```

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

OTHER NAMES:

CN 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline

CN AZD 2171

CN Cediranib

CN ZD 2171

DR 790713-41-6, 557795-03-6

MF C25 H27 F N4 O3

CI COM

SR CA

LC STN Files: ADISINSIGHT, CA, CAPLUS, CASREACT, CHEMCATS, CSCHEM, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, PROUSDDR, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

87 REFERENCES IN FILE CA (1907 TO DATE)

5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

87 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil caplus COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 7.88 8.10

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 13:30:39 ON 13 JUL 2009 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 13 Jul 2009 VOL 151 ISS 3
FILE LAST UPDATED: 12 Jul 2009 (20090712/ED)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2009

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2009

CAplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2009.

CAS Information Use Policies apply and are available at:

http://www.cas.org/legal/infopolicy.html

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> 11

L2 87 L1

 $\Rightarrow$  12 and py<2005

25140894 PY<2005

L3 5 L2 AND PY<2005

=> d 13 ibib abs 1-5

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:995977 CAPLUS

DOCUMENT NUMBER: 141:420417

TITLE: Therapeutic agents comprising an anti-angiogenic agent

in combination with an Src inhibitor for use in

normotensive treatment of angiogenesis

INVENTOR(S): Curwen, Jon Owen; Wedge, Stephen Robert

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PA:	PATENT NO.					D	DATE			APPL	ICAT	ION 1	ΝΟ.		D.	ATE		
WO	2004	0986	04		A1		2004	1118		WO 2	004-	GB19	39		2	0040	504	<
	W:	ΑE,	AG,	AL,	AM,	ΑT,	AU,	AZ,	BΑ,	BB,	ВG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	KΖ,	LC,	
										MG,								
								,		RU,								
										US,								
	RW:	BW,																
			•			•				AT,								
	EE, ES, F] SI, SK, TF					•	•											
				SK, TR, BF, BJ,			CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MK,	ΝE,	
7. 1.1	SN, TD, TG J 2004237132				7. 1		2004	1110		7.11.7	004	2271	2.2		2	0040	E O 4	,
	2004						2004			AU Z	004-	Z3 / 1.	32		۷	0040	304	<
_	2519	_	-							CA 2	004-	2510	03 N		2	<b>n</b> n 4 n	504	/
	1620									EP 2								
111		AT,																
	10.									BG,							/	
BR	2004									BR 2							504	
CN	R 2004009742 N 17 <b>8</b> 4232									CN 2								
CN							2008											
JP	TP 2006525304				T		2006	1109		JP 2	006-	5062	22		2	0040	504	
NZ	Z 542348				А		2009	0131		NZ 2	004-	5423	48		2	0040	504	

NO 2005004411	A	20051130	NO 2005-4411		20050923
ZA 2005008858	A	20070328	ZA 2005-8858		20051101
US 20060223815	A1	20061005	US 2005-555389		20051103
MX 2005011858	A	20060217	MX 2005-11858		20051104
PRIORITY APPLN. INFO.:			GB 2003-10401	A	<b>20</b> 030 <b>5</b> 07
			WO 2004-GB1939	M	20040504

GΙ

AΒ The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965067 CAPLUS

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving

cell proliferation, migration or apoptosis of myeloma

cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin

Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,

Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;

Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

```
PATENT NO.
                                 KIND
                                            DATE
                                                            APPLICATION NO.
                                                                                             DATE
       _____
                                  ____
                                             _____
                                                             _____
                                                                                              _____
                                                            WO 2004-EP4363
                                                                                               20040424 <--
       WO 2004096224
                                   A2
                                             20041111
       WO 2004096224
                                   A3
                                             20041216
            W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
            W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, MIL, MR, NE,
                  SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
                  SN, TD, TG
                                             20041103
       EP 1473043
                                                            EP 2003-9587
                                                                                               20030429 <--
                                    Α1
            R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                  IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
       AU 2004233576
                                             20041111 AU 2004-233576
                                                                                               20040424 <--
                                   A1
       CA 2523868
                                             20041111
                                                              CA 2004-2523868
                                                                                               20040424 <--
                                    Α1
       EP 1622619
                                    Α2
                                             20060208
                                                              EP 2004-729366
                                                                                               20040424
                AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                  IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
       BR 2004009919
                                    Α
                                           20060425
                                                            BR 2004-9919
                                                                                               20040424
       JP 2006524634
                                    Τ
                                             20061102
                                                              JP 2006-500099
                                                                                               20040424
       MX 2005011656
                                            20051215
                                                              MX 2005-11656
                                   Α
                                                                                              20051028
       NO 2005005605
                                    Α
                                             20051128
                                                              NO 2005-5605
                                                                                              20051128
PRIORITY APPLN. INFO.:
                                                              EP 2003-9587
                                                                                         A 20030429
                                                                                         A 20040113
                                                              EP 2004-508
                                                              EP 2004-1171
                                                                                          A 20040121
                                                                                     W 20040424
                                                              WO 2004-EP4363
```

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2003:532545 CAPLUS

DOCUMENT NUMBER: 139:95455

TITLE: Combined therapy against tumors comprising substituted

acryloyl distamycin derivatives and protein kinase

(serine/threonine kinase) inhibitors

INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo

PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent English LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	TENT NO.		KINI	D D2	ATE			APPL	ICAT	ION	NO.		D.	ATE			
	20030555 W: AE, CO, GM, LS, PL, UG, RW: GH, KG,	AG, A CR, C HR, I LT, I PT, I US, U	AL, CU, HU, LU, RO, UZ, KE,	A1 AM, CZ, ID, LV, RU, VC, LS, RU,	20 AT, 2 DE, 1 IL, 3 MA, 1 SD, 3 VN, 3 MW, 1 TJ, 3	003 AU, DK, IN, MD, SE, YU, MZ,	0710 AZ, DM, IS, MG, SG, ZA, SD, AT,	BA, DZ, JP, MK, SK, ZM, SL, BE,	WO 2 BB, EC, KE, MN, SL, ZW SZ, BG,	BG, EE, KG, MW, TJ,	EP13 BR, ES, KP, MX, TM,	092 BY, FI, KR, MZ, TN,	BZ, GB, KZ, NO, TR,	2 CA, GD, LC, NZ, TT, AM, DK,	GE, LK, OM, TZ, AZ, EE,	CN, GH, LR, PH, UA, BY, ES,	
		CG,													Dr,	DU,	
AU AU EP	2472008 20023520 20023520 1461083 1461083	90	·	A1 A1 B2 A1	2) 2) 2)	003 003 008 004	0710 0715 0515 0929		CA 2 AU 2	002- 002-	2472 3520	008 90	·	2			
	R: AT,								GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,	
	IE,	SI, I	LT,	LV,	FI, I	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	SK			
	20020154				_				^		0.000			^			<
CN	20040026 1617744 20055160	139		AΖ	21	005	0420 0518		n∪ 2	004-	2039 8276	74		2	00212 00213	210 218	
JP	20055160	25		T	21	005	0602		JP 2	003-	5560	98		2	0021	218	
AT	321572			T T3	2	006	0415		AT 2	002-	7877	63		2	00212	218	
ES	2263835			Т3	2	006	1216		ES 2	002- 002-	7877	63		2	00212	218	
	533854			A C2	21	007	1216 0531 0710		NZ 2	002-	5338	54		2			
RU	2328306			C2	21	800	0710		RU 2	004- 004-	1236	41		2	00212		
	20040065	43		A A	21		1004		MX 2	004 - 004 -	6543			2	0040	702	<
	20040052 2004DN01	90		A A	21	005	0617 0403			004-							
	2004DN03				21					004-							<
	20060084				2					005-							`
	2007DN00				2					007-							
PRIORITY	Y APPLN.	INFO.	:						EP 2	002-	7505	2	2	A 2	0020	102	
										002-							
									IN 2	004-	DN19	60	1	A3 2	0040	708	
OTHER SO	OURCE(S):			MARI	PAT 1	39:	9545	5									

GΙ

AB The present invention provides the combined use of acryloyl distamycin derivs., in particular  $\alpha$ -bromo- and  $\alpha$ -chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:747609 CAPLUS

DOCUMENT NUMBER: 135:283196

TITLE: Therapeutic combinations of antihypertensive and

antiangiogenic agents

INVENTOR(S): Curwen, Jon Owen; Ogilvie, Donald James

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND DA	DATE APP	PLICATION NO.	DATE
WO 2001074360	A1 20	20011011 WO	2001-GB1522	20010402 <
W: AE, AG,	L, AM, AT, A	AU, AZ, BA, BE	B, BG, BR, BY, BZ	, CA, CH, CN,
CO, CR,	U, CZ, DE, I	DK, DM, DZ, EE	E, ES, FI, GB, GD	, GE, GH, GM,
HR, HU,	D, IL, IN, I	IS, JP, KE, KG	G, KP, KR, KZ, LC	, LK, LR, LS,
LT, LU,	V, MA, MD, N	MG, MK, MN, MW	, MX, MZ, NO, NZ	, PL, PT, RO,
RU, SD,	E, SG, SI, S	SK, SL, TJ, TM	I, TR, TT, TZ, UA	, UG, US, UZ,
VN, YU,	A, ZW			
RW: GH, GM,	E, LS, MW, N	MZ, SD, SL, SZ	I, TZ, UG, ZW, AT	, BE, CH, CY,
DE, DK,	S, FI, FR, (	GB, GR, IE, II	C, LU, MC, NL, PT	, SE, TR, BF,

```
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                          CA 2001-2401854
                              20011011
    CA 2401854
                        A1
                                                                20010402 <--
    EP 1272186
                        Α1
                              20030108
                                          EP 2001-917305
                                                                20010402 <--
                        В1
                              20070228
    EP 1272186
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    BR 2001009729
                       A
                              20030204
                                          BR 2001-9729
                                                                20010402 <--
    HU 2003000426
                              20030628
                                          HU 2003-426
                                                                20010402 <--
                       A2
    JP 2003528917
                       Τ
                              20030930 JP 2001-572104
                                                                20010402 <--
    EE 200200578
                              20040615 EE 2002-578
                                                                20010402 <--
                       Α
                      B2
                                                                20010402
    AU 2001244386
                              20050127
                                       AU 2001-244386
    NZ 520938
                       Α
                              20050826 NZ 2001-520938
                                                                20010402
                              20060315 AT 2001-917305
    AT 355065
                       T
                                                                20010402
                                        EP 2006-3576
    EP 1658849
                       A2
                              20060524
                                                                20010402
                       A3
    EP 1658849
                              20090218
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                              20070126
    NZ 534455
                        Α
                                          NZ 2001-534455
                                                                20010402
    EP 1790340
                                          EP 2007-3863
                                                                20010402
                        Α2
                              20070530
    EP 1790340
                        A3
                              20090318
        R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC,
            NL, PT, SE, TR, AL, LT, LV, MK, RO, SI
    ES 2280349
                        Т3
                              20070916
                                          ES 2001-917305
                                                                20010402
    CZ 299410
                        В6
                              20080716
                                          CZ 2002-3304
                                                                20010402
    IN 2002MN01149
                        Α
                              20050304
                                          IN 2002-MN1149
                                                                20020823
    ZA 2002006959
                              20031201
                                          ZA 2002-6959
                        Α
                                                                20020829 <--
                              20030731
                                          US 2002-240413
    US 20030144298
                        Α1
                                                                20021001 <--
                        B1
    KR 849149
                              20080731
                                        KR 2002-713170
                                                                20021002
                       A
    MX 2002009743
                              20030327
                                        MX 2002-9743
                                                                20021003 <--
    NO 2002004814
                       A
                              20021112
                                         NO 2002-4814
                                                                20021004 <--
                       B1 20070521
    NO 323467
                              20011008
                       A
    NO 2006002050
                                         NO 2006-2050
                                                                20060508 <--
    NO 326277
                       B1
                              20081027
    KR 2008034523
                       A
                              20080421
                                          KR 2008-707835
                                                                20080331
PRIORITY APPLN. INFO.:
                                          GB 2000-8269
                                                            A 20000405
                                          EP 2001-917305
                                                            A3 20010402
                                          NZ 2001-520938
                                                            A1 20010402
                                          WO 2001-GB1522
                                                             W 20010402
                                          KR 2002-713170
                                                             A3 20021002
OTHER SOURCE(S):
                       MARPAT 135:283196
    The invention concerns the use of a combination of an anti-angiogenic
    agent and an anti-hypertensive agent for use in the manufacture of a medicament
    for the treatment of a disease state associated with angiogenesis in a
    warm-blooded mammal, such as a human being. The invention also relates to
    pharmaceutical compns. comprising an anti-angiogenic agent and an
    anti-hypertensive agent, to kits thereof and to a method of treatment of a
    disease state associated with angiogenesis which comprises the administration
    of an effective amount of a combination of an anti-angiogenic agent and an
    anti-hypertensive agent to a warm-blooded animal, such as a human being.
```

blood pressure was reversed by the addition of captopril. REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ylmethoxy)quinazoline for 10 days, then they were dosed orally with 30

mg/kg captopril in addition to quinazoline compound The increase in diastolic

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN ACCESSION NUMBER: 2000:573671 CAPLUS

Anesthetized rats were dosed orally with 12.5 mg/kg of

4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-

DOCUMENT NUMBER: 133:177183

TITLE: Preparation of quinazoline derivatives as angiogenesis

inhibitors

INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick;

Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren

PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.

SOURCE: PCT Int. Appl., 346 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
		WO 2000-GB373	
W: AE, AL, AM,	AT, AU, AZ, BA,	BB, BG, BR, BY, CA, CH,	CN, CR, CU,
		GB, GD, GE, GH, GM, HR,	
IN, IS, JP,	KE, KG, KP, KR,	KZ, LC, LK, LR, LS, LT,	LU, LV, MA,
MD, MG, MK,	MN, MW, MX, NO,	NZ, PL, PT, RO, RU, SD,	SE, SG, SI,
SK, SL, TJ,	TM, TR, TT, TZ,	UA, UG, US, UZ, VN, YU,	ZA, ZW
RW: GH, GM, KE,	LS, MW, SD, SL,	SZ, TZ, UG, ZW, AT, BE,	CH, CY, DE,
DK, ES, FI,	FR, GB, GR, IE,	IT, LU, MC, NL, PT, SE,	BF, BJ, CF,
CG, CI, CM,		MR, NE, SN, TD, TG	
CA 2362715		CA 2000-2362715	
EP 1154774		EP 2000-902730	20000208 <
EP 1154774	B1 20050622		
		GB, GR, IT, LI, LU, NL,	SE, MC, PT,
IE, SI, LT,	LV, FI, RO		
TR 200102314	T2 20020121	TR 2001-2314	20000208 <
BR 2000008128 HU 2001004964 HU 2001004964	A 20020213		20000208 <
HU 2001004964	A2 20020429	HU 2001-4964	20000208 <
HU 2001004964	A3 20030228		
JP 2002536414	T 20021029		20000208 <
JP 3893026	B2 20070314	0001 100	0000000
EE 200100409	A 20021216		20000208 <
AU /63618	B2 20030731		20000208 <
EE 200100409 AU 763618 NZ 513204 CN 1167422	A 20040430		20000208 <
CN 116/422	C 20040922		
CN 1597667 CN 100360505 TR 200500745 NZ 530832	A 20050323 C 20080109	CN 2004-10058982	20000208
TP 200500745	T2 20050523		20000208
N7 530832	7 20050525	NZ 2000-530832	20000200
EP 1553097	A1 20050713		
		GB, GR, IT, LI, LU, NL,	
	LV, FI, RO, MK,		5E, FC, II,
AT 298237	T 20050715		20000208
RU 2262935	C2 20051027	RU 2001-124816	20000208
	T3 20051027	ES 2000-902730	20000208
IL 144745	A 20081103	IL 2000-144745	
IL 144745 EP 2050744	A1 20090422	EP 2008-168638	20000208
R: AT, BE, CH,	CY, DE, DK, ES,	FI, FR, GB, GR, IE, IT,	
	AL, LT, LV, MK,		,,,
IN 2000DE00115			20000211
IN 2001MN00893	A 20070525	IN 2001-MN893	20010726
ZA 2001006340	A 20021101	ZA 2001-6340	20010801 <
NO 2001003882	A 20011009	NO 2001-3882	20010809 <
NO 321604	B1 20060612		
MX 2001008182	A 20030820	MX 2001-8182	20010810 <
KR <b>83861</b> 7	B1 20080616	KR 2001-710133	20010810
HK 1041212	A1 20051202	HK 2002-102781	20020412
US 7074800	B1 20060711	US 2002-913020	20020506
NO 2005002773	A 20011009	NO 2005-2773	20050608 <

US 20060004017	A1	20060105	US	2005-169122		20050629
HK 1076104	A1	20081031	HK	2005-108262		20050921
JP 2006273860	A	20061012	JP	2006-129249		20060508
KR 2008015482	A	20080219	KR	2007-731001		20071231
PRIORITY APPLN. INFO.:			EP	1999-400305	A	19990210
			EP	2000-902730	A3	20000208
			EP	2005-4285	A3	20000208
			JP	2000-598164	A3	20000208
			WO	2000-GB373	W	20000208
			KR	2001-710133	A3	20010810
			US	2002-913020	A3	20020506

OTHER SOURCE(S):

MARPAT 133:177183

GΙ

The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered AΒ bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = 0, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl, alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

ΙI

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 13 ibib abs 1-5 hitstr

L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:995977 CAPLUS

DOCUMENT NUMBER: 141:420417

TITLE: Therapeutic agents comprising an anti-angiogenic agent

in combination with an Src inhibitor for use in

normotensive treatment of angiogenesis Curwen, Jon Owen; Wedge, Stephen Robert

Astrazeneca AB, Swed.; Astrazeneca UK Limited PATENT ASSIGNEE(S):

PCT Int. Appl., 111 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

INVENTOR(S):

PAT	PATENT NO.						DATE			APPL						ATE		
WO	2004	 0986	04													0040	 504 <-	
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BW,	BY,	ΒZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,	
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,	
							PL,											
							TZ,											
	RW:	,	,	,	,	,	MW,			,	,	,	,	,	,	,		
							RU,											
																	SE,	
		SI,	SK,	TR,	BF,	вJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GO,	GW,	ML,	MR,	NE,	
		SN,			•	·	·	·	·	·	·	·	~ ,	,	,	,	,	
AU	2004	2371 2371	32		A1		2004	1118		AU 2	004-	2371	32		2	0040	504 <	
		2004237132 2519930																
CA	2519	930			A1		2004	1118		CA 2	004-	2519	930		2	0040	504 <	
EP	1620	104			A1		2006	0201		EP 2	004-	7310	49		2	0040	504	
	R:	AT,	ΒE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙT,	LI,	LU,	NL,	SE,	MC,	PT,	
		ΙE,	SI,	LT,	LV,	FI,	RO,	CY,	TR,	BG,	CZ,	EE,	HU,	PL,	SK,	HR		
BR	2004	0097	42		A		2006	0509		BR 2	004-	9742			2	0040	504	
CN	1784	232			A		2006	0607		CN 2	004-	8001	2089		2	0040	504	
CN	1784 1004 2006	1853	1		С		2008	0917										
JP	2006	5253	04		T		2006	1109		JP 2	006-	5062	22		2	0040	504	
NZ	5423	48			A		2009	0131		NZ 2	004-	5423	48		2	0040	504	
NO	2005	0044	11		A		2005	1130		NO 2	005-	4411			2	0050	923	
ZA	2005	8800	58		A		2007	0328		ZA 2	005-	8858			2	0051	101	
US	2006	0223	815		A1		2006	1005		US 2	005-	5553	89		2	0051	103	
MX	2005	0118	58		A		2006	0217		MX 2	005-	1185	8		2	0051	104	
CIORITY	Y APP	LN.	INFO	.:						GB 2	003-	1040	1		A 2	0030	507	
										WO 2	004-	GB19.	39		W 2	0040	504	
•																		

AΒ The invention relates to the use of an anti-angiogenic agent, such as I (preparation given), in combination with an inhibitor of the Src family of non-receptor tyrosine kinases, such as the II (prepns. according to a previous patent given), in the manufacture of a medicament for use in the substantially normotensive treatment in a warm-blooded mammal such as a human being of a disease state associated with angiogenesis. The invention provides for the Src kinase inhibitor to be administered in an amount effective to counteract substantially the hypertension induced by the anti-angiogenic agent. Thus, 7-(2-chloroethoxy)-4-(6-chloro-2,3methylenedioxyanilino)-5-isopropoxyquinazoline was coupled with 1-acetylpiperazine using KI in DMA to give I. The diastolic blood pressure profile of rats over a 24 h period after administration of a combination of 1.5 mg/kg of I and 25 mg/kg of II demonstrated that the contrasting blood pressure effects of the antiangiogenic agent and the Src kinase inhibitor were substantially counterbalanced.

IT 288383-20-0, 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (angiogenesis inhibitor; therapeutic agents comprising an anti-angiogenic agent in combination with an Src inhibitor for use in normotensive treatment of angiogenesis)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:965067 CAPLUS

DOCUMENT NUMBER: 141:406039

TITLE: Combinations for the treatment of diseases involving

cell proliferation, migration or apoptosis of myeloma

cells, or angiogenesis

INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin

Friedrich; Baum, Anke; Munzert, Gerd; Van Meel,

Jacobus C. A.

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany;

Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PA	PATENT NO.					)	DATE		,						D.	ATE		
	20040											EP43			2	0040	424 <-	-
	( : : 1	CN, GH, LR, NZ,	CO, GM, LS, OM,	CR, HR, LT, PG,	CU, HU, LU, PH,	CZ, ID, LV, PL,	AU, DK, IL, MA, PT, UA,	DM, IN, MD, RO,	DZ, IS, MG, RU,	EC, JP, MK, SC,	EE, KE, MN, SD,	EG, KG, MW, SE,	ES, KP, MX, SG,	FI, KR, MZ, SK,	GB, KZ, NA, SL,	GD, LC, NI, SY,	GE, LK, NO,	
	1	AZ, EE, SI,	BY, ES,	KG, FI, TR,	KZ, FR,	MD, GB,	MW, RU, GR, CF,	TJ, HU,	TM, IE,	AT, IT,	BE, LU,	BG, MC,	CH, NL,	CY, PL,	CZ, PT,	DE, RO,	DK, SE,	
EP	14730	43	·		A1		2004	1103		EP 2	003-	9587			2	0030	429 <-	
	R: 2		•	•	•		ES, RO,	•			•						PT,	
	20042																	
_	25238									_								
EP	16226																	
		ΙE,	SI,	FΙ,	RO,	CY,	TR,	ВG,	CZ,	EE,	HU,	PL,	SK	·			·	
	20040						2006											
	20065																	
	20050																	
NO PRIORIT	20050 Y APPLI				А		2005	1128		EP 2	003-	9587			A 2	0051: 0030: 0040:	429	

EP 2004-1171 A 20040121 WO 2004-EP4363 W 20040424

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

IT 288383-20-0

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(drug combinations for diseases involving cell proliferation and migration or apoptosis or angiogenesis including protein tyrosine kinase receptor antagonists and radiotherapy)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2003:532545 CAPLUS

DOCUMENT NUMBER: 139:95455

TITLE: Combined therapy against tumors comprising substituted

acryloyl distamycin derivatives and protein kinase

(serine/threonine kinase) inhibitors

INVENTOR(S): Geroni, Maria Cristina; Fowst, Camilla; Cozzi, Paolo

PATENT ASSIGNEE(S): Pharmacia Italia SpA, Italy

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.	KIND DATE	APPLICATION NO.	DATE
WO 2003055522	A1 2003071	0 WO 2002-EP13092	20021218 <
W: AE, AG, AL,	AM, AT, AU, AZ	, BA, BB, BG, BR, BY, B	Z, CA, CH, CN,
CO, CR, CU,	CZ, DE, DK, DM	, DZ, EC, EE, ES, FI, GH	3, GD, GE, GH,
GM, HR, HU,	ID, IL, IN, IS	, JP, KE, KG, KP, KR, KZ	Z, LC, LK, LR,
LS, LT, LU,	LV, MA, MD, MG	, MK, MN, MW, MX, MZ, NO	), NZ, OM, PH,
PL, PT, RO,	RU, SD, SE, SG	, SK, SL, TJ, TM, TN, TH	R, TT, TZ, UA,

```
UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2472008
                                20030710
                                             CA 2002-2472008
                                                                     20021218 <--
                          Α1
     AU 2002352090
                          A1
                                 20030715
                                             AU 2002-352090
                                                                     20021218 <--
     AU 2002352090
                          В2
                                 20080515
                                             EP 2002-787763
     EP 1461083
                          A1
                                 20040929
                                                                     20021218 <--
     EP 1461083
                          В1
                                 20060329
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     BR 2002015454
                          Α
                                20041123
                                             BR 2002-15454
                                                                     20021218 <--
     HU 2004002639
                          A2
                                20050428
                                             HU 2004-2639
                                                                     20021218
     CN 1617744
                                20050518
                                             CN 2002-827674
                                                                     20021218
                          Α
     JP 2005516025
                                20050602
                                             JP 2003-556098
                          Τ
                                                                     20021218
     AT 321572
                                             AT 2002-787763
                          Τ
                                20060415
                                                                     20021218
     ES 2263835
                                             ES 2002-787763
                          Т3
                                20061216
                                                                     20021218
     NZ 533854
                                             NZ 2002-533854
                                20070531
                                                                     20021218
                          Α
     RU 2328306
                          C2
                                20080710
                                             RU 2004-123641
                                                                     20021218
     MX 2004006543
                          Α
                                20041004
                                             MX 2004-6543
                                                                     20040702
     ZA 2004005290
                          Α
                                 20050617
                                             ZA 2004-5290
                                                                     20040702
     IN 2004DN01960
                          Α
                                 20090403
                                             IN 2004-DN1960
                                                                     20040708
                                             NO 2004-3217
     NO 2004003217
                                20040730
                                                                     20040729 <--
                          Α
                                             US 2005-500606
                                 20060420
     US 20060084612
                          Α1
                                                                     20050505
     IN 2007DN00991
                          Α
                                20070803
                                             IN 2007-DN991
                                                                     20070206
PRIORITY APPLN. INFO.:
                                             EP 2002-75052
                                                                 A 20020102
                                             WO 2002-EP13092
                                                                  W
                                                                    20021218
                                             IN 2004-DN1960
                                                                 A3 20040708
OTHER SOURCE(S):
                        MARPAT 139:95455
```

Br
H2C=C-CO-NH

Me
CO-NH

Me
CO-NH

Me
CO-NH

Me
CO-NH

N

Me
CO-NH-CH2 CH2 NH-C-NH2

NH

GΙ

AΒ

The present invention provides the combined use of acryloyl distamycin

derivs., in particular  $\alpha$ -bromo- and  $\alpha$ -chloro-acryloyl distamycin derivs., and a protein kinase (serine/threonine and tyrosine kinases) inhibitor, in the treatment of tumors. Also provided is the use of the said combinations in the treatment or prevention of metastasis or in the treatment of tumors by inhibition of angiogenesis. An example protein kinase inhibitor is STI 571 and a distamycin derivative is brostallicin (I).

IT 288383-20-0, ZD 2171

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combined antitumor therapy comprising acryloyl distamycin derivs. and protein kinase (serine/threonine kinase) inhibitors)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

$$N - (CH_2)_3 - O$$
 $MeO$ 
 $N$ 
 $F$ 
 $N$ 
 $MeO$ 
 $N$ 
 $M$ 
 $M$ 
 $M$ 
 $M$ 
 $M$ 

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2001:747609 CAPLUS

DOCUMENT NUMBER: 135:283196

TITLE: Therapeutic combinations of antihypertensive and

antiangiogenic agents

INVENTOR(S): Curwen, Jon Owen; Ogilvie, Donald James

PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAT	ATENT NO. 				KIN	D	DATE			APPL	ICAT	ION :	NO.		D.	ATE	
WO	2001	0743	 60		A1		2001	1011		WO 2	001-	GB15	22		2	0010	402 <
	W:	ΑE,	AG,	AL,	AM,	AT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,	GM,
		HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,	LS,
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	PL,	PT,	RO,
		RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,
		VN,	YU,	ZA,	ZW												
	RW:	GH,	GM,	KE,	LS,	MW,	MΖ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,
		DE,	DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	TR,	BF,
		ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG		
CA	2401	854			A1		2001	1011		CA 2	001-	2401	854		2	0010	402 <
EP	1272	186			A1		2003	0108		EP 2	001-	9173	05		2	0010	402 <
EP	1272	186			В1		2007	0228									
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR						

```
BR 2001009729
                      A
                                                              20010402 <--
                             20030204 BR 2001-9729
    HU 2003000426
                      A2
                             20030628 HU 2003-426
                                                              20010402 <--
                       T
                                                              20010402 <--
    JP 2003528917
                             20030930 JP 2001-572104
    EE 200200578
                       Α
                             20040615 EE 2002-578
                                                              20010402 <--
    AU 2001244386
                      В2
                             20050127 AU 2001-244386
                                                              20010402
    NZ 520938
                      A
                             20050826 NZ 2001-520938
                                                              20010402
    AT 355065
                       T
                             20060315 AT 2001-917305
                                                              20010402
    EP 1658849
                      A2
                             20060524
                                       EP 2006-3576
                                                              20010402
    EP 1658849
                       А3
                            20090218
          AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    NZ 534455
                             20070126
                                         NZ 2001-534455
                       Α
    EP 1790340
                        A2
                              20070530
                                         EP 2007-3863
                                                              20010402
                             20090318
    EP 1790340
                       A3
        R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC,
            NL, PT, SE, TR, AL, LT, LV, MK, RO, SI
                             20070916
                                         ES 2001-917305
    ES 2280349
                       Т3
    CZ 299410
                                         CZ 2002-3304
                        В6
                             20080716
                                                              20010402
    IN 2002MN01149
                                         IN 2002-MN1149
                                                              20020823
                       Α
                             20050304
    ZA 2002006959
                             20031201
                                         ZA 2002-6959
                                                              20020829 <--
                       Α
    US 20030144298
                       A1
                             20030731
                                         US 2002-240413
                                                              20021001 <--
                            20080731
                                         KR 2002-713170
    KR 849149
                       В1
                                                              20021002
    MX 2002009743
                             20030327
                        Α
                                         MX 2002-9743
                                                              20021003 <--
    NO 2002004814
                       Α
                             20021112
                                        NO 2002-4814
                                                              20021004 <--
                       B1 20070521
    NO 323467
    NO 2006002050
                       A
                             20011008
                                        NO 2006-2050
                                                              20060508 <--
                       В1
                             20081027
    NO 326277
    KR 2008034523
                       A
                             20080421
                                         KR 2008-707835
                                                              20080331
                                                          A 20000405
PRIORITY APPLN. INFO.:
                                         GB 2000-8269
                                                          A3 20010402
                                         EP 2001-917305
                                         NZ 2001-520938
                                                           A1 20010402
                                                           W 20010402
                                         WO 2001-GB1522
                                         KR 2002-713170
                                                           A3 20021002
```

OTHER SOURCE(S): MARPAT 135:283196

The invention concerns the use of a combination of an anti-angiogenic agent and an anti-hypertensive agent for use in the manufacture of a medicament for the treatment of a disease state associated with angiogenesis in a warm-blooded mammal, such as a human being. The invention also relates to pharmaceutical compns. comprising an anti-angiogenic agent and an anti-hypertensive agent, to kits thereof and to a method of treatment of a disease state associated with angiogenesis which comprises the administration of an effective amount of a combination of an anti-angiogenic agent and an anti-hypertensive agent to a warm-blooded animal, such as a human being. Anesthetized rats were dosed orally with 12.5 mg/kg of 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4ylmethoxy)quinazoline for 10 days, then they were dosed orally with 30 mg/kg captopril in addition to quinazoline compound The increase in diastolic blood pressure was reversed by the addition of captopril. ΤТ 288383-20-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(therapeutic combinations of antihypertensive and antiangiogenic agents)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1pyrrolidinyl)propoxy]- (CA INDEX NAME)

$$N - (CH_2)_3 - O$$
 $MeO$ 
 $N$ 
 $F$ 
 $N$ 
 $MeO$ 
 $N$ 
 $MeO$ 
 $N$ 
 $M$ 
 $M$ 
 $M$ 

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2000:573671 CAPLUS

DOCUMENT NUMBER: 133:177183

TITLE: Preparation of quinazoline derivatives as angiogenesis

inhibitors

INVENTOR(S): Hennequin, Laurent Francois Andre; Ple, Patrick;

Stokes, Elaine Sophie Elizabeth; Mckerrecher, Darren

PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Zeneca-Pharma S.A.

SOURCE: PCT Int. Appl., 346 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.																		
WO											2000-							<
	W:	ΑE,	AL,	AM,	ΑT,	ΑU,	AZ,	ΒA,	BB,	ВG	, BR,	BY,	CA,	CH,	CN,	CR,	CU,	,
		CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD	, GE,	GH,	GM,	HR,	HU,	ID,	IL,	,
		IN,	IS,	JP,	ΚE,	KG,	KΡ,	KR,	ΚZ,	LC	, LK,	LR,	LS,	LT,	LU,	LV,	MA,	,
		MD,	MG,	MK,	MN,	MW,	MX,	NO,	NΖ,	PL	, PT,	RO,	RU,	SD,	SE,	SG,	SI,	,
		SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG	, US,	UΖ,	VN,	YU,	ZA,	ZW		
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	TZ	, UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,	,
		DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU	, MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	,
											, SN,							
CA	2362	715			A1		2000	0817	(	CA	2000-	2362	715		2	0000	208	<
										EΡ	2000-	9027	30		2	0000	208	<
EΡ	1154																	
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,	,
		,	,	,	LV,	,												
TR	2001	0231	4		Т2		2002			TR	2001-	2314			2	0000	208	<
BR	2000	0081	28		A		2002		]	BR	2000-	8128			2	0000	208	<
HU	2001	0049	64		A2				1	HU	2001-	4964			2	0000	208	<
	2001						2003											
	2002	5364	14		${f T}$		2002		· ·	JΡ	2000-	5981	64		2	0000	208	<
_	3893				В2		2007											
EE	2001	0040	9		A		2002	-			2001-					0000		
AU	7636 5132	18			В2		2003				2000-					0000		
NZ	5132	04			A		2004				2000-							
CN	1167	422			С		2004				2000-							<
CN	1597	667			A		2005		(	CN	2004-	1005	8982		2	0000	208	
	1003		5		С		2008											
	2005		5		Т2		2005			TR	2005-	745			2	0000	208	
NZ	5308	32			А		2005	0527	1	NZ	2000- 2005-	5308	32		2	0000	208	
ΕP																		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,	

	IE, Si	I, LT,	LV,	FI, RO, MK,	CY, AL			
AT	298237		T	20050715	AT 2000-902730		20000208	
RU	2262935		C2	20051027	RU 2001-124816		20000208	
ES	2242596		Т3	20051116			20000208	
$_{ m IL}$	144745		A	20081103	IL 2000-144745		20000208	
EP	2050744		A1	20090422	EP 2008-168638		20000208	
	R: AT, B	E, CH,	CY,	DE, DK, ES,	FI, FR, GB, GR, IE,	IT, LI	í, LU, MC,	
			ΑL,	LT, LV, MK,				
	2000DE0011		Α				20000211	
	2001MN00893	3	Α	20070525			20010726	
	2001006340		Α	20021101			20010801	
_	2001003882		Α	20011009			20010809	<
_	321604		В1	20060612				
	2001008182		A	20030820			20010810	<
	838617		В1	20080616			20010810	
	1041212		A1	20051202			20020412	
	7074800		В1	20060711			20020506	
	2005002773		A	20011009			20050608	<
	2006000401	7	A1	20060105			20050629	
	1076104		A1	20081031			20050921	
	2006273860		A	20061012			20060508	
	2008015482		A	20080219			20071231	
PRIORIT	Y APPLN. INI	<b>:</b> 0.:			EP 1999-400305		19990210	
					EP 2000-902730	А3	20000208	
					EP 2005-4285	_	20000208	
					JP 2000-598164		20000208	
					WO 2000-GB373	W	20000208	
					KR 2001-710133	A3	20010810	
					US 2002-913020	А3	20020506	

OTHER SOURCE(S): MARPAT 133:177183

AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl,

alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

IT 288383-20-0P, 4-(4-Fluoro-2-methylindol-5-yloxy)-6-methoxy-7-[3-(pyrrolidin-1-yl)propoxy]quinazoline

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(angiogenesis inhibitor; preparation of quinazolines as angiogenesis inhibitors by cyclization of 2-aminobenzamides and subsequent derivatization)

RN 288383-20-0 CAPLUS

CN Quinazoline, 4-[(4-fluoro-2-methyl-1H-indol-5-yl)oxy]-6-methoxy-7-[3-(1-pyrrolidinyl)propoxy]- (CA INDEX NAME)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT